

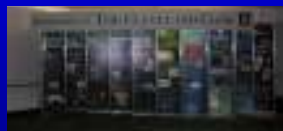


Nephron- Sparing Treatments for Renal Tumors

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March 22nd, 2006





What are the intermediate results of MIS Partial Nx?

What's an adequate margin for a partial Nx?


What is the most recent data on Cryo and RFA?

Should we do partial Nx for T1b tumors?

Did Fenster just take the last doughnut?



Overview

- History
 - Open Partial Nephrectomy
 - MIS Partial Nephrectomy
 - Cryoablation
 - Radiofrequency Ablation (RFA)
- 

History of Partial Nx



Czerny



Simon

- 1869- Gustav Simon
 - 1st planned Nx
- 1884- Wells
 - 1st Partial Nx (accidentally)
- 1887- Vincenz Czerny
 - 1st planned Partial Nx

19th C 1900 1910 1920 1930 1940 1950 1960 1970 1980 1990 2000

History of Partial Nx

- 1879- 1900:
 - Tillman, Tuffier, Bardenheuer, Paoli
 - experimental feasibility studies
 - Lost favor: fear of Cx



Tuffier in action

19th C 1900 1910 1920 1930 1940 1950 1960 1970 1980 1990 2000

History of Partial Nx

- 1901-1935: Goldstein and Abeshouse
 - 296 cases, 34 for tumors
 - Polar small-moderate tumors
 - "... contraindicated if opposite kidney was healthy." JU 38:15,1937.



19 th C	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000
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History of Partial Nx

- 1950- Vermooten
 - Foundation of modern NSS
 - Autopsy studies (Bell, Hale)
 - Proposed elective NSS

"There are certain instances, when it is unwise to do a nephrectomy... The question is, whether such a procedure is ever justifiable when the opposite kidney is normal. I am inclined to think that in certain circumstances it may be."

JU 64:200, 1950.



19 th C	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000
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History of Partial Nx

- 1960s: Significant improvements in NSS
 - Poutasse: segmental blood supply
 - Kerr and Klotz: renal hypothermia
- Partial Nx done in essential cases



19 th C	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000
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History of Partial Nx

- mid 1970s:
- Question Rad Nx even if normal contralateral kidney
 - Puigvert
 - Herr
 - Novick
 - Marberger



19 th C	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000
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History of Partial Nx

- 1981: Era of elective NSS
 - CT scan detection
 - Kidney reconstruction
 - Renal hypothermia
- Hotly debated



19 th C	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000
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History of Partial Nx

- Late 1990s: Standard of Care
 - Improved hemostasis techniques
 - Long term data (10 yr)
 - Herr 1999
 - Fergany 2000



19 th C	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000
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History of Nephron-Sparing Tx

- MIS Partial Nx
 - 1993- Winfield: 1st case for LP tic
 - 1994- Gill: RP MIS Partial Nx
- Cryoablation
 - 1995– Uchida: 1st report
 - 1998– Gill: MIS Cryo
- RFA
 - 1997– Zlotta: 1st report
 - 2000-2002: early percutaneous experience



19 th C	1900	1910	1920	1930	1940	1950	1960	1970	1980	1990	2000
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Nephron-Sparing Tx: Indications

- **Absolute** (“Imperative”)
 - Solitary kidney
 - Bilateral tumors
 - Severe renal insufficiency
- **Relative**
 - Contralateral kidney threatened by:
 - Local conditions: (eg. stones, infxn, RAS, UPJO)
 - Systemic conditions: (eg. DM, HTN)
 - Genetic conditions: (eg. vHL)
- **Elective (Normal Contralateral Kidney)**
 - Small (<4 cm; ? <7 cm)
 - Young





Open Partial Nephrectomy

Open Partial Nx- Techniques

- Enucleation
- Polar segmental resection
- Wedge resection
- Major transverse resection
- Ex vivo resection & autotransplant



Technique Overview

- Approach
- Inspection of kidney
- Isolation of vessels
- Cytoprotection
- Adequate resection
- Hemostasis & closure



Technique- Warm Ischemia

WIT (min)	Immed Renal Fxn Loss (%)	Recovery of Renal Fxn
10	Minimal	Complete, min
20	40-50	Complete, hrs
30	60-70	Complete, 3-9d
60	70-80	Often complete, wks
120	100	Incomplete (30-50%)
180	100	None

- 30 min WIT

(Novick Urol Clin NA 1983,
Maessan Transplantation 1988.)

- 90 min (porcine)

(Laven JU 172: 2471,2004.)

- Solitary kidney
- ↓ GFR initial 72 hr
- GFR normal @ 2 wks
 - @ 1 wk (Baldwin Uro 2004)



Ward BJU 47:17,1975.

Technique– Warm Ischemia

- More functional impairment if:
 - Clamp artery & vein (vs. artery alone) Nadelhaft 1981.
 - Intermittent (vs. continuous) Wilson 1971
 - Manual compression (vs. clamp) McLaughlin 1978
- Enhanced renal tolerance:
 - Solitary kidney
 - Collateral blood supply



Technique– Renal Hypothermia

- Optimum temp 15°C
 - Canine experiments by Ward 1975
- 20-25 °C easier to maintain
 - Renal protection for **90 min to 3 hr** (Novick 1983)
- Renal surface hypothermia (most common)
- Perfusion hypothermia (equal efficacy)



Technique— Margins

DOES THE SIZE OF THE SURGICAL MARGIN IN PARTIAL NEPHRECTOMY FOR RENAL CELL CANCER REALLY MATTER?

SUZETTE E. SUTHERLAND, MARTIN I. RESNICK,* GREGORY T. MACLENNAN AND HOWARD B. GOLDMAN

JU 167:61, 2002

- 44 open partial Nx— 41 negative surgical margins
- 49 mo mean f/u
- No local recurrence @ resection site
- Median margin size: **2 mm**
- 42 of 44 cases: <5 mm margin



Technique- Hemostasis

- Suture closure vessels & collecting system
- Argon beam coagulation
- Thrombotic agents:
 - Gelfoam
 - Tisseal
 - FloSeal
 - Surgicel



Complications

1995-6 National Surgical Adjuvant Breast and Bowel Intestinal (NSABO) B-31 trial results

Measure	Rad Nx	Partial Nx	Rad Nx	Partial Nx	Rad Nx	Partial Nx	Rad Nx	Partial Nx	Rad Nx	Partial Nx
Recurrence	28%	28%	-	28%	28%	-	28%	28%	28%	28%
Local recurrence	22%	22%	-	22%	22%	-	22%	22%	22%	22%
Distant recurrence	18%	18%	-	18%	18%	-	18%	18%	18%	18%
Death	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
Death due to cancer	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%
Death due to cause other than cancer	4%	4%	4%	4%	4%	4%	4%	4%	4%	4%
Quality of life	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
Side effects	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%
Total	12%	12%	12%	12%	12%	12%	12%	12%	12%	12%

Uzzo & Novick JU 2004

NSS Results– Renal Fxn

- Lau et al. JU 163 (Supp 4):153, 2000.
 - Mayo clinic, n=1730 pt
 - Unilateral RCC w/ normal contralat kidney
 - Rad Nx vs. Partial Nx
 - Matched TNM, grade, tumor size, year
 - Progression to renal insuff. (Cr > 2mg/dl)
 - **12.4% Rad Nx**
 - **2.3% Partial Nx** (p<0.002)

Open Partial Nx- Results

TABLE 2. Outcome in patients undergoing nephron sparing surgery for sporadic renal cell carcinoma

References	No. Pts.	% Disease Specific Survival	% Local Recurrence	Mean Followup (mos.)
Jacobs et al ¹⁴⁰	51	84	10	60
Marberger et al ¹⁹⁰	72	78	8	Not available
Smith et al ¹⁸⁴	39	72	8	Not available
Marshall and Walsh ⁸⁵	10	90	10	24.5
Bazeed et al ¹⁹⁰	51	96	4	35.8
Carini et al ¹⁸¹	35	80	3	45.8
Gohji et al ¹⁸⁶	21	100	0	Not available
Morgan and Zinde ¹⁸²	104	80	6	60
Selli et al ¹⁸³	56	90	4	46.2
Provet et al ¹⁸	44	88	2	36
Steinbach et al ¹⁶	121	90	4.1	47
Moll et al ²¹	142	98	1.4	34.8
Thrasher et al ¹⁴⁷	21	100	0	40
Lerner et al ¹⁸	185	80	5.9	44
D'Armiento et al ⁶⁷	19	95	0	70
Indudhara et al ¹⁸³	35	100	0	37
van Poppel et al ¹⁴⁸	76	96	0	75
Hafez et al ²⁷	485	92	3.2	47
Barbalias et al ⁶⁸	41	97.5	7.3	59
Belldegrun et al ²⁵	146	93	2.7	74
Lee et al ²⁰	79	96	0	40
Total (range)	1,833	(72-100)	(0-10)	(24-75)

> 90% in recent series



Uzzo & Novick JU 2001

Results- Elective NSS

Reference	No. Pts.	% Disease Specific Survival	% Local Recurrence	Mean Followup (mos.)	Survival Rate (%)
Marberger et al ¹⁹⁰	72	78	8	60	60
Smith et al ¹⁸⁴	39	72	8	Not available	70
Marshall and Walsh ⁸⁵	10	90	10	24.5	60
Bazeed et al ¹⁹⁰	51	96	4	35.8	60
Carini et al ¹⁸¹	35	80	3	45.8	60
Gohji et al ¹⁸⁶	21	100	0	Not available	60
Morgan and Zinde ¹⁸²	104	80	6	60	60
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D'Armiento et al ⁶⁷	19	95	0	70	60
Indudhara et al ¹⁸³	35	100	0	37	60
van Poppel et al ¹⁴⁸	76	96	0	75	60
Hafez et al ²⁷	485	92	3.2	47	60
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Belldegrun et al ²⁵	146	93	2.7	74	60
Lee et al ²⁰	79	96	0	40	60
Total (range)	1,833	(72-100)	(0-10)	(24-75)	(60-60)

Long-term Results

- Fergany. JU 163:442, 2000.
 - CCF, sporadic RCC
 - N=107
 - 90% partial Nx imperative indications
 - Min. 10 yr f/u
- Herr. JU 161:33,1999.
 - MSK
 - N=70
 - Small tumors w/ normal contralat kidney
 - Mean size: 3 cm
 - Mean f/u: 10 yrs
 - 97 % cancer free survival

	% 5 Yr survival	% 10 Yr survival
Overall	88.2	73
< 4cm	98	92



Partial vs Radical Nx

References	Nephrectomy/Nephron Sparing Surgery	
	No. Pts.	% Cancer Specific 5-Yr. Survival
Lerner et al ¹⁸	209/185	89/89
Barbalias et al ⁶⁸	48/41	98.4/97.5
Belldegrun et al ²³	125/108	91.2/96
Indudhara et al ⁸³	71/85	94/91
Butler et al ¹⁷	42/46	97/100
D'Armiento et al ⁶⁷	21/19	96/96
Lee et al ²⁰	183/79	95/95

- Retrospective
- Controlled for:
 - Age
 - Gender
 - Tumor size
 - Stage
 - Grade



Tumor Location

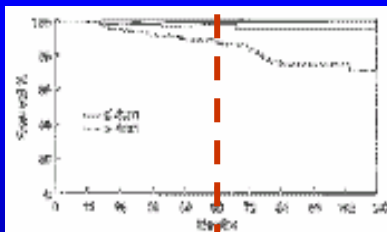
- Central vs peripheral
- Technical considerations
 - Longer clamp time
 - Collecting system repair
- Not prognostic indicator of outcome
 - Renal function
 - Local tumor recurrence
 - 5 yr cancer specific survival

Hafez et al JU 159:1156, 1998.

Black et al JU 163: 737, 2000.



Tumor Size: 4 cm cutoff



5 yr cancer-specific survival 96% vs 86% (p=0.001)

- Hafez et al. JU 162: 1930, 1999.
 - CCF, 485 patients
 - 4 cm cutoff
 - Lower recurrence rate
 - 5% vs. 16% (p=0.001)
 - Not T1a vs T1b though
 - 50 of 175 pts in >4cm group were >T1
 - No control group undergoing Rad Nx



Partial vs Rad Nx: 4-7 cm

- Leibovich et al.

JU 171:1066,2004.

	NSS	Rad Nx
5 yr cancer specific survival	98 %	86%
5 yr recurrence free survival	93%	98%

- Mayo Clinic
- Retrospective
- Heterogeneous:
 - Mean tumor size
 - TNM path stage
 - Histo subtype



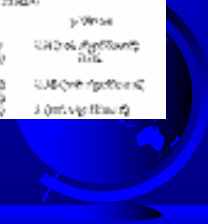
Partial vs Rad Nx– T1a/b

SAFETY AND EFFICACY OF PARTIAL NEPHRECTOMY FOR ALL T1 TUMORS BASED ON AN INTERNATIONAL MULTICENTRE EXPERIENCE

Patard et al. JU 171:2185,2004.

- 7 international centers (Europe & UCLA)
- n= 1454, pathological T1
- Mean f/u: 62.5 mo

	Europe	UCLA	UCLA	UCLA	UCLA	UCLA
Mean follow-up (mo)	62.5	62.5	62.5	62.5	62.5	62.5
Mean tumor size (cm)	3.5	3.5	3.5	3.5	3.5	3.5
Mean age (yr)	62.5	62.5	62.5	62.5	62.5	62.5
Mean f/u (mo)	62.5	62.5	62.5	62.5	62.5	62.5
Mean tumor size (cm)	3.5	3.5	3.5	3.5	3.5	3.5
Mean age (yr)	62.5	62.5	62.5	62.5	62.5	62.5
Mean f/u (mo)	62.5	62.5	62.5	62.5	62.5	62.5



Open Partial vs Radical Nx- T1a/b Cancer Specific Survival

T1a

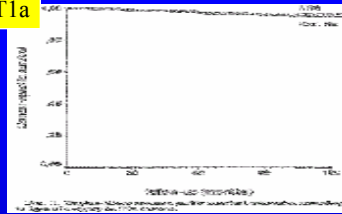


TABLE 2. Cancer specific survival according to tumor size and type of surgery

Tumor Size	Radical Nephrectomy	Open Partial Nephrectomy	p Value
T1a	10 (100%)	10 (100%)	0.95
T1b	10 (100%)	10 (100%)	0.97
T1a+b	20 (100%)	20 (100%)	0.96

T1b

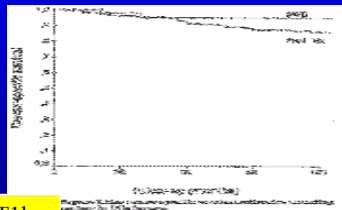


TABLE 3. Cancer specific survival according to tumor size and type of surgery

Tumor Size	Radical Nephrectomy	Open Partial Nephrectomy	p Value
T1a	10 (100%)	10 (100%)	0.95
T1b	10 (100%)	10 (100%)	0.97
T1a+b	20 (100%)	20 (100%)	0.96

Open Partial vs Rad Nx- T1a/b Recurrence

TABLE 3. Analysis of type of recurrence according to tumor size and type of surgery

	No. T1a Tumors (%)	No. T1b Tumors (%)
No. partial nephrectomy (p = 0.2)	10 (100%)	10 (100%)
No recurrence	9 (90%)	9 (90%)
Local recurrence	1 (10%)	1 (10%)
Distant recurrence	0 (0%)	0 (0%)
No. radical nephrectomy (p = 0.001)	10 (100%)	10 (100%)
No recurrence	10 (100%)	179 (82.1)
Local recurrence	0 (0%)	5 (2.8)
Distant recurrence	0 (0%)	34 (15.6)
p Value	0.9 (not significant)	0.5 (not significant)

Partial Nx:
T1a vs T1b
No difference

T1a: Partial
vs Radical Nx
No difference

T1b: Partial
vs Radical Nx
No difference

NSS- Local Recurrence

- Incomplete resection of tumor
- Occult multifocal disease
- Development of new 1° or metastatic focus



Results– Multifocal RCC

Table 6. Survival of multifocal renal cell carcinoma

Subgroup	No.	No. at Risk	Event	Recurrence Rate	5-Year Overall Survival Rate (%)
All patients	100	100	26	26%	48%
Non-metastatic	70	70	14	20%	64%
Metastatic	30	30	12	40%	24%
Stage I	30	30	5	17%	73%
Stage II	20	20	7	35%	50%
Stage III	20	20	2	10%	70%
Stage IV	10	10	8	80%	10%
Subtotal	100	100	26	26%	48%

Stage, grade, histological subtype

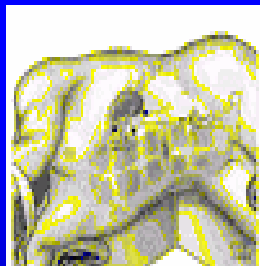
Open Partial Nx– Results Summary

- NSS for T1a (<4cm)
 - Equivalent oncological efficacy
 - 90-100% cancer specific survival
 - Renal function preserved
 - Multifocal RCC: 5%
 - Local Recurrence: 0-7%
- ? Expand indications to T1b

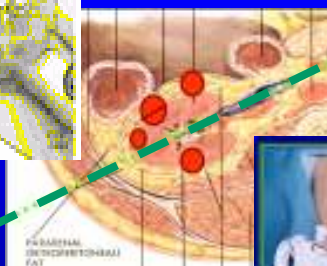


Laparoscopic Partial Nephrectomy

Technique– Approach



Transperitoneal



Retroperitoneal



Laparoscopic Ultrasound




- Endophytic, central
- Lower positive margin
 - 14% vs. 3%
Wash U: Am J Surg 171(4 suppl), 2004
- ? Multifocal tumor
 - No advantage compared to pre-op CT
Campbell et al. JU 155:1991, 1996.

Technique- Hypothermia

- If expect WIT >30 min
- Surface contact renal hypothermia
 - Endocatch II bag (Gill et al. JU 170:52,2003.)
- Intra-arterial iced RL (Janetschek. JU 171,2004)
 - Angiocath into renal artery via femoral
- Retrograde endoscopic
 - Ureteral access sheath (Landman. Urology 2003)



Technique- Hilar Clamping

- Montsouris, France. JU 169:483,2003. 
- Retrospective, n=28
- Group 1 (no clamp, ultrasonic & bipolar)
- Group 2 (clamp, ureteral catheter cooling)

	Group 1	Group 2	p-value
Time to renal reperfusion (min)	25.1 ± 1.7 (n=14)	25.1 ± 1.7 (n=14)	0.99
Time to renal reperfusion (min)	25.1 ± 1.7 (n=14)	25.1 ± 1.7 (n=14)	0.99
Time to renal reperfusion (min)	25.1 ± 1.7 (n=14)	25.1 ± 1.7 (n=14)	0.99
Time to renal reperfusion (min)	25.1 ± 1.7 (n=14)	25.1 ± 1.7 (n=14)	0.99

Technique– Hemostasis

- Tourniquets (w/o hilar clamping)
 - Regional hypoperfusion
 - Cable-tie, double-loop & Vicryl mesh
 - Peripheral/polar tumors
 - **Unreliable**
- Argon beamer
- Tissue sealants
 - ↓ hemorrhage & urine leak (Spaliviero.CCF. JU 171(4 suppl),2004)



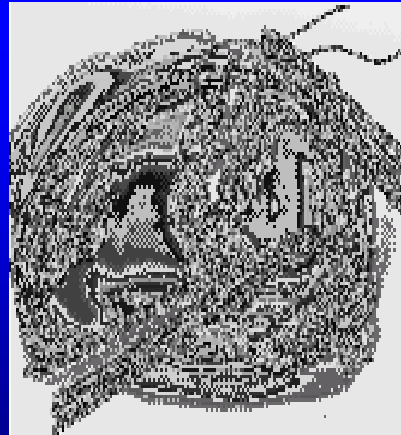
Technique- Hemostasis

- Coagulative Energy
 - Animal studies: Water-Jet dissector, Laser
 - Suboptimal: Ultrasonic, Bipolar, Microwave
 - RF Coagulation: peripheral tumor
(Winfield J Endo 2005; Cadeddu AUAUS 2004)
- **Standard: Suture closure reconstruction**
 - Especially larger & central lesions



Technique- Closure

- Watertight closure collecting system
- Vessels
- Floseal
- Surgicel 'cigar'
- Sutures w/ Hem-o-Lok clips or LapraTy



MIS- Complications

	Se Peng 00	Se Peng 00	Se Peng 00	Total 200
Central lysis	1 (0.5%)	1 (0.5%)	1 (0.5%)	3 (1.5%)
Open conversion	1 (0.5%)	1 (0.5%)	1 (0.5%)	3 (1.5%)
Ureteral injury	1 (0.5%)	1 (0.5%)	1 (0.5%)	3 (1.5%)
Bladder injury	1 (0.5%)	1 (0.5%)	1 (0.5%)	3 (1.5%)
Rectal injury	1 (0.5%)	1 (0.5%)	1 (0.5%)	3 (1.5%)
Small bowel injury	1 (0.5%)	1 (0.5%)	1 (0.5%)	3 (1.5%)
Other	1 (0.5%)	1 (0.5%)	1 (0.5%)	3 (1.5%)
Total	7 (3.5%)	7 (3.5%)	7 (3.5%)	21 (10.5%)

Ramani. JU 173:42,2005.

- CCF. n=200, 25% central, 71% pelvicaliceal repair
- 7.5% solitary, Open conversion in 1%
- Floseal: ↓ hemorrhage to 3%, ↓ urine leak to 1.5%

Gill et al. Uro 65,2005.

MIS- Central Tumors

- Conversion
 - Open Partial (1)
 - MIS Rad Nx (1)
- Early Post-Op Cx
 - Hemorrhage (3.9%)
 - Urine leak (1.3%)

	Central	Peripheral
N	154	209
Size (cm)	3.0 (1-7)	2.4 (0.7-10)
WIT(min)	33.5	30
+ Margin	0.8%	0.7%
IntraOp Cx	5.2%	4.8%
Early Postop	5.8%	1.9%
Late Postop	7.8%	7.7%

Frank. CCF. JU 175:849, 2006.

MIS– Oncological Results

	CCF <small>JU 175:459,2006</small>	Hopkins <small>JU 172:871,2004</small>
No RCC	68	48
F/U (mo)	42	37
Size (cm)	2.9	2.4
# Pos Margins	1	1
Cancer-specific survival (%)	100	100
# local recurrences	0	2 (1 vHL, 1 remote)

COMPARATIVE ANALYSIS OF LAPAROSCOPIC VERSUS OPEN PARTIAL NEPHRECTOMY FOR RENAL TUMORS IN 200 PATIENTS



- Gill vs Novick.
JU 170:64, 2003.
- Retrospective
- Post-op renal fxn
 - No difference

	MIS	Open
† Size (cm)	2.8	3.3
† Solitary	41%	54%
† WIT (min)	27.8	17.5
† EBL (cc)	125	250
† IntraOp Cx	5%	0%
† GU Cx	11%	2%
Pos Margin	3%	1%
† LOS (days)	2	5

MIS Partial Nx– Summary

- Technically challenging
- Technique evolving
- Intermediate oncological efficacy similar
- Vs. Open:
 - ↑ Intraoperative Cx
 - ↑ GU Cx





Ablation

Ablation– Indications

- Advanced age
- Limited life expectancy
- High operative risk/ Refuse surgery
- Multifocal RCC (eg. vHL)
- Solitary kidney
- Small (<3 cm), exophytic



Ablation Options

- **Cryoablation**
 - Open
 - MIS
 - Percutaneous
- Thermal Ablation
 - **Radiofrequency Ablation (RFA)**
 - High Intensity Focused Ultrasound (HIFU)
 - Microwave
 - Laser Induced Thermotherapy (LITT)
 - Interstitial Photon Radiation Ablation



Cryoablation

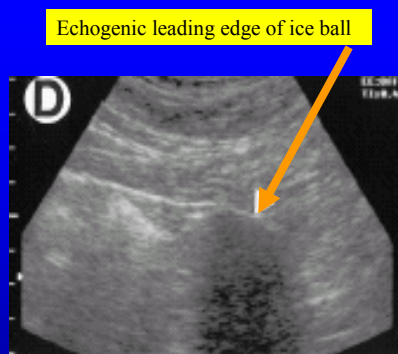
Cryoablation- Mechanism

- Direct cytotoxic injury:
 - Intracellular ice crystals → Hyperosmolar environment
 - Cell dehydration, shrinkage, enzyme denaturation, cytoskeleton & membrane dysfunction
- Indirect ischemic injury
 - Occlusion of local tissue microvasculature
- “Freeze/ Thaw” cycle (Wooley et al. J Endourology 16:519,2002)
 - Rapid freeze, then gradual thaw
 - Maximizes effect



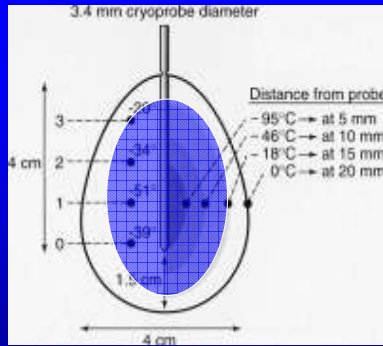
Cryoablation– Technique

- Approach
- Imaging
- Bx
- 2.4 -4.8 mm cryoprobe
- Double freeze/ thaw
 - Freeze: Liquid N or Ar
 - Thaw: Passive, He gas



Gill JU 173: 1903, 2005. Nadler JU 170:1121, 2003. Gupta JU 175:447, 2006.

Cryoablation- Ice Ball

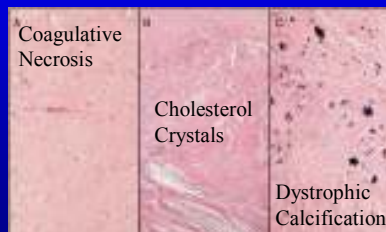


- -19.4°C needed
- U/S, CT, or MRI
- Ice ball overrepresents actual area of ablation
- Aim for ice ball 1 cm greater than tumor
 - Minimum 3.1 mm
(Campbell et al. Urology 52:29, 1998)

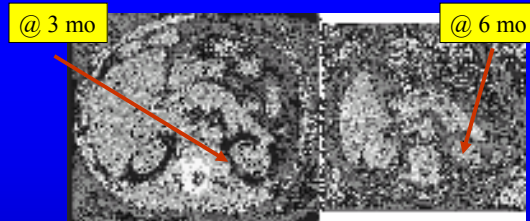
Chosy JU 159:1370,1998. Gill JU 173: 1903, 2005.

Cryoablation- Efficacy

- Confirmed tumoricidal effects
 - Acute (Edmunds et al. J Endourol 14:139,2000.)
 - Chronic (Jang et al. JU 173:720, 2005.)



Post Cryoablation Imaging



- CT or MRI
- Non-enhancing
 - Transient rim enhancement @ 1-3 mo
 - Bx: no RCC
 - ? Reactive changes
- Same or decrease in size



Shingleton. JU 165,2001. Gill. JU 173:1903,2005.

Shrinkage



Shrinkage

Mean Tumor Size (cm)	Standard Deviation (cm)	Mean Tumor Size (cm)	Standard Deviation (cm)	Mean Tumor Size (cm)	Standard Deviation (cm)
1.0	0.2	1.0	0.2	1.0	0.2
1.5	0.3	1.5	0.3	1.5	0.3
2.0	0.4	2.0	0.4	2.0	0.4
2.5	0.5	2.5	0.5	2.5	0.5
3.0	0.6	3.0	0.6	3.0	0.6
3.5	0.7	3.5	0.7	3.5	0.7
4.0	0.8	4.0	0.8	4.0	0.8
4.5	0.9	4.5	0.9	4.5	0.9
5.0	1.0	5.0	1.0	5.0	1.0
5.5	1.1	5.5	1.1	5.5	1.1
6.0	1.2	6.0	1.2	6.0	1.2

@ 2 hrs



@ 30 days



Cryoablation- Results

RENAL CRYOABLATION: OUTCOME AT 3 YEARS

INDERBIR S. GILL,*† ERICK M. REMER, WALEED A. HASAN, BRENDA STRZEMPKOWSKI, MASSIMILIANO SPALIVIERO, ANDREW P. STEINBERG, JIHAD H. KAOUK, MIHIR M. DESAI AND ANDREW C. NOVICK

JU 173:1903,2005.

- 56 pts w/ 3 yr f/u
- Mean tumor size: 2.3 cm (1-5 cm)
- 2 lesions (3.6%) abutting collecting system
- Routine 6 mo post-op Bx in 39 pts (70%)



MIS Cryo 3 yr f/u

- 98% 3 yr cancer-specific survival
- 2 local recurrences (5.6%)
 - Neg routine Bx
 - New MRI enhancement
- Renal fxn– no change

MIS Cryo 3 yr f/u		
	T9L	T9R
Age	29	19
Sex	Female	Female
Weight	160	160
Height	160	160
MI	0	0
HTN	0	0
DM	0	0
Cholesterol	170	170
Triglycerides	170	170
Glucose	100	100
Albumin	4.0	4.0
BUN	10	10
Cr	1.0	1.0
Calcium	10.0	10.0
Phosphorus	3.0	3.0
Sodium	140	140
Potassium	4.0	4.0
Magnesium	2.0	2.0
Iron	50	50
Zinc	100	100
Copper	100	100
Selenium	100	100
Manganese	100	100
Cadmium	100	100
Lead	100	100
Mercury	100	100
Barium	100	100
Strontium	100	100
Yttrium	100	100
Zirconium	100	100
Niobium	100	100
Molybdenum	100	100
Technetium	100	100
Ruthenium	100	100
Rhodium	100	100
Palladium	100	100
Silver	100	100
Cadmium	100	100
Mercury	100	100
Barium	100	100
Strontium	100	100
Yttrium	100	100
Zirconium	100	100
Niobium	100	100
Molybdenum	100	100
Technetium	100	100
Ruthenium	100	100
Rhodium	100	100
Palladium	100	100
Silver	100	100

Percutaneous Cryoablation

- MRI guided
 - Shingleton and Sewell. Mississippi. JU 165:773,2001.
 - 22 tumors, 20 pts
 - Mean tumor size: 3 cm (1.8-7 cm)
 - No OR Bx, 2 or 3 mm probe, 3 freeze-thaw
 - Anterior location 20% -- no bowel injuries
 - Mean f/u: 9.1 mo (3-14)
 - No recurrences
 - (1 pt retreated b/c VHL)



Shingleton

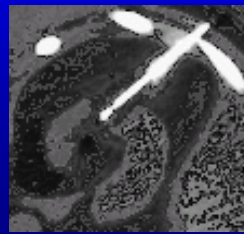


Percutaneous Cryoablation

- CT guided
 - Hopkins. JU 175:447, 2006.
 - N=27 lesions (20 pts)
 - Conscious sedation
 - Size: 2.5 cm
 - 1 pt required pRBC
 - 16 lesions f/u 6 mo
 - 15/16 no enhancement
 - Small, non-central lesions
- U/S guided
 - Bassignani JU 171, 2004.
 - N=4
 - GA
 - No periop Cx



Su



Complications

- Major/ Bleeding (<1%) JU 172:874,2004.
 - Use smaller probes
 - Refreeze
 - Floseal, Surgicel, Argon beam
- Pain/Paresthesia @ probe site
- ?Collecting system
 - Initial prostate cryoablation: urethral sloughing





Radiofrequency Ablation (RFA)

RFA– Mechanism



- High frequency electrical current
- Excitation ions
- Frictional heat
- Denature proteins & membrane bilayer
- Need tissue temp $>50^{\circ}\text{C}$



RFA– Technique

- Open, MIS, Perc
- Difficult to image RFA effect during Tx
- 200 W, Probe tip temp 105-110°C
- Reduce tissue impedance:
 - Wet RFA
 - Internal cooling (CoolTip probe)
 - Multiple tine electrodes
 - Temperature sensing; Impedance monitoring



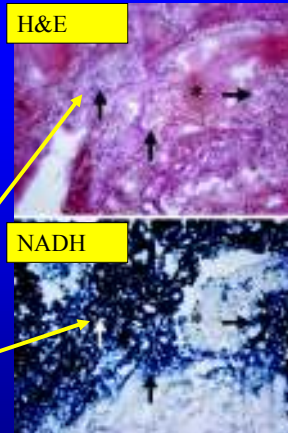
RFA– Ablate & Resect

- Rendon et al. UofT. JU 167:1587,2002.
 - RFA then immediate or delayed Nx
 - Mean size: 2.4 cm, N= 11 lesions
 - **Viable tumor** on pathology (H&E):
 - 4 of 5 in acute group
 - 3 of 6 in delayed group
 - 5-10 % viable tumor at margins of Tx areas
 - Non-enhancing lesions: 2 of 3 had tumor
 - 100 W probe, ? Tissue temp



RFA– Ablate & Resect

- Michaels. Lahey Clinic.
 - 15 patients, 20 tumors
 - Open RFA → immediate Partial Nx
 - Size: 2.4 cm (1.5-3.5 cm)
 - H&E: All 20 — viable tumor w/in RFA lesion
 - NADH:
 - 4 of 5 viable tumor



JU 168:2406, 2002.

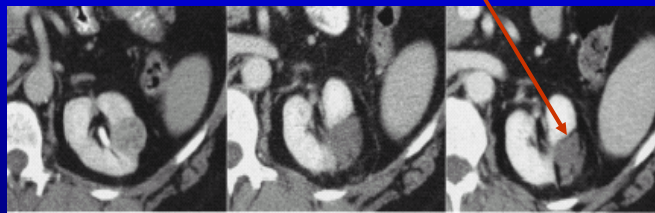
RFA– Histological Effect

- “Viable” tumor foci early post RFA
 - Full effect of RFA may require more time
 - Cellular changes continue 30-90 days post-RFA
- Accuracy of H&E:
 - Overt histo destruction may not be seen acutely
- **NADH**: cell viability (Marcovich et al. LIJ. JU Oct 2003.)
- No long-term post-RFA histo studies

Gill. Urology 56:197,2000.

RFA— Postablation Imaging

- Low density, wedge-shaped
- Minimal shrinkage
- Fibrotic halo of fat (exophytic)
- Fat infiltration (50%) (endophytic)



Matsumoto. JU 172:45,2004

RFA— Early data

	Date	N	Size (cm)	F/U (mo)	'Success'
Ogan	2002	13	2.4	4.9	93% (CT)
Pavlovich	2002	24	<3	2	79% (CT)
Roy- Choudhury	2002	15	3.0	13.6	87%
Su	2003	35	1.9	3.2	95% (CT)
Gervais	2003	42	3.2	42	100% exophytic 5/11 central

RFA– New Data

- Matsumoto et al. SouthWestern. JU 172:45,2004.
 - 64 tumors, Perc(34)/ MIS(28)/ Open(2)
 - F/u 13.7 mo
 - 97% (62/64) nonenhancing



Cadeddu



RFA– New Data

- Hwang et al. NIH. JU 171:1814, 2004.
 - 17 pts, hereditary RCC, 24 tumors
 - 2.26 cm
 - F/U: 1 year
 - 23 of 24 (96%) non-enhancing post RFA



RFA– New Data

- Gervais et al. MGH.

AJR.185:64,2005.

- 100 tumors
- CT-guided percutaneous RFA
- Size: 3.2 cm (1.1-8.9 cm)
- Mean F/U: 2.3 yrs
- 90% non-enhancing post RFA



Gervais



McDougal



Gervais et al. 2005

- Location:
 - Exophytic– 100% (67/67)
 - Central– 78% (7/9)
 - Mixed– 61% (11/18)
- Size:
 - <3 cm: 100% (4/52 needed 2 RFA sessions)
 - 3-5 cm: 92% (17/36 needed 2 or 3 RFA sessions)
 - >5 cm: 25% (2/2 needed 2 or 3 RFA sessions)
 - Note: no tumors >5.5 cm completely ablated



RFA– Complications

Johnson. JU 172:874,2004. Gervais AJR:185,2005.

- Low morbidity (9.2% minor Cx)
 - Most common: pain/paraesthesia @ probe site
- <2% major Cx:
 - Bleeding, UPJ obstruction, urine leak
- No bowel injury
 - Patient selection
 - 7 bowel perms in 3500 RFA liver Radiology 226:441, 2003.



RFA– Complications

- ?Collecting system (Janzen. UCLA. JU 173/11368, 2005)
 - Swine model
 - High rate urothelial damage acutely (60-90%)
 - @ 30 days, intact urothelium
 - No clinical fistula/urinoma
- 2% ureteral injury (Gervais AJR 185,2005)



RFA– Summary

- <3 cm
- Non-central
- Minimal morbidity
- Early f/u: >90 % recurrence free
- Multiple RFA treatments may be needed



Cryo vs RFA

- | | |
|--|--|
| <ul style="list-style-type: none">• ↓ intraoperative pain• Monitor ice ball• Confirmed acute & chronic tumor kill• ? ↓ collecting system injury | <ul style="list-style-type: none">• More hemostatic• Lower cost• ↓ probe site pain |
|--|--|



Gupta JU 2006. Collyer J Am Coll Surg 193:2001.

